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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,175	08/06/2003	Nila Patil	200/1004-40	9177
31662	7590	12/21/2005	EXAMINER	
PERLEGEN SCIENCES, INC. LEGAL DEPARTMENT 2021 STIERLIN COURT MOUNTAIN VIEW, CA 94043			BERTAGNA, ANGELA MARIE	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/635,175

Applicant(s)

PATIL ET AL.

Examiner

Angela Bertagna

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 9-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-15 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date: <u>2/12/04; 7/19/04; 9/27/04; 3/1/05</u> | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restrictions

1. Claims 7 and 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 21, 2005.

Priority

2. It is noted that this application appears to claim subject matter disclosed in prior Application Nos. 60/228,251, filed August 26, 2000; 09/768,936, filed January 23, 2001; 09/938,878, filed August 24, 2001; and 10/131,832, filed April 24, 2002. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference **must include the relationship** (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or

after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its

inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Accordingly, priority has not been granted, and the prior art has been applied with respect to the filing date of the instant application (August 6, 2003).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 1-6 and 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Deugau et al. (US Patent No. 5,508,169).

With regard to claim 1, Deugau et al. disclose a method of analyzing nucleic acids using the polymerase chain reaction (PCR), comprising:

- a. Providing a double-stranded population of nucleic acids comprising single-stranded overhangs (see column 5, line 50 – column 6, line 12; Example 2, columns 17-18)
- b. Annealing ligate linkers to said population of nucleic acids whereby at least a subset of nucleic acids from said double-stranded population have linkers bound at both ends (column 6, lines 1-12; column 7, lines 1-5; Example 2, columns 17-18)
- c. Amplifying said subset of nucleic acids by PCR, thereby analyzing said subset of nucleic acids (column 6, lines 1-12; column 7, lines 1-5; Example 2, columns 17-18).

Note that the “indexing linkers” of Deugau et al. have as an essential element a “double-stranded oligonucleotide with a first end having a protruding single strand of 3, 4, or 5 nucleotides, and having a second end having a protruding single strand of any number of nucleotides, including zero” (column 6, lines 39-46). These “indexing linkers” are ligated to the single-stranded overhangs in the nucleic acid population and are therefore a functional equivalent of the instantly claimed “ligate linkers”. This disclosure of Deugau et al. meets the limitations of the instant claim 1.

With regard to claim 2, Deugau et al. disclose the use of genomic lambda phage DNA (column 17, lines 65-67), thereby meeting the instant limitation that said population of nucleic acids is a population of genomic DNA fragments.

With regard to claim 3, Deugau et al. disclose that said single-stranded overhangs are derived from restriction enzyme digestions (see column 5, line 50 – column 6, line 12; Example 2, columns 17-18).

With regard to claim 4, Deugau et al. disclose that said ligate linkers comprise a common PCR primer binding site (Example 2, column 18, lines 5-39).

With regard to claim 5, Deugau et al. disclose that said ligate linkers comprise a different PCR primer binding site for each overhang (Example 4, column 20-21).

With regard to claim 6, Deugau et al. disclose that said restriction enzyme is selected from the group consisting of a single Type IIs restriction enzyme, a combination of two or more Type IIs enzymes, and a combination of Type IIs restriction enzymes and other types of restriction enzymes. Specifically, Deugau et al. disclose the use of FokI, a Type IIs restriction enzyme (Example 2, column 18, lines 1-5).

With regard to claim 9, Deugau et al. disclose a method of analyzing a subset of nucleic acids within a nucleic acid population using the polymerase chain reaction (PCR), comprising:

- a. Providing a double-stranded population of nucleic acids that comprise cleaved interrupted palindromic sequences at one or both ends (see column 5, line 50 – column 6, line 12)
- b. Annealing an adaptor containing fixed nucleotides onto said population of nucleic acids thereby producing at least a subset of nucleic acids that comprise an adaptor sequence at both ends (column 6, lines 1-12; column 7, lines 1-5)
- c. Amplifying said subset of nucleic acids by PCR, thereby analyzing said subset of nucleic acids (column 6, lines 1-12; column 7, lines 1-5).

Note that the “indexing linkers” of Deugau et al. have as an essential element a “double-stranded oligonucleotide with a first end having a protruding single strand of 3, 4, or 5 nucleotides, and having a second end having a protruding single strand of any number of nucleotides, including zero” (column 6, lines 39-46). These “indexing linkers” are ligated to the single-stranded overhangs in the nucleic acid population and are therefore a functional equivalent of the instantly claimed “adaptor”. This disclosure of Deugau et al. meets the limitations of the instant claim 9.

With regard to claim 10, Deugau et al. disclose that said subset of nucleic acids comprises nucleic acid fragments of a first size (Example 4, column 20, lines 22-40). The term “a first size” has been interpreted to mean a specific size resulting from digestion of the subset within the initial population with a restriction enzyme. Deugau et

al. disclose fragmentation of an initial population of nucleic acids containing interrupted palindromic sequences, with an interrupted palindrome recognizing enzyme (SfiI), thereby producing a subset of nucleic acids comprising nucleic acid fragments of a first size (191 bp and 102 bp fragments), and meeting the limitations of the instant claim.

With regard to claim 11, Deugau et al. disclose that said interrupted palindromic sequences are interrupted by at least one ambiguous nucleotide (column 5, lines 50-65). By definition, an "interrupted palindromic sequence" is interrupted by at least one ambiguous nucleotide (see for example page 2 of http://www.promega.com/guides/re_guide/chapone/1_2.htm). Therefore, the use of cleaved interrupted palindromic sequences by Deugau et al. inherently meets the limitations of the instant claim.

With regard to claim 12, Deugau et al. disclose that said cleaved interrupted palindromic sequences are derived from restriction enzyme digestions (column 5, lines 50-65; column 7, lines 41-46).

With regard to claim 13, Deugau et al. disclose that said restriction enzyme is a single restriction enzyme or a combination of two or more restriction enzymes (column 5, lines 50-65; column 7, lines 41-46).

With regard to claim 14, Deugau et al. disclose that said adaptor comprises a single-stranded overhang that has at least one fixed nucleotide (column 9, lines 4-21).

With regard to claim 15, Deugau et al. disclose that said adaptor comprises a PCR primer binding site (column 7, lines 1-5).

5. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong et al. (WO/0024939) and 35 U.S.C. 102(e) as being anticipated by Dong et al. (US Patent No. 6,361,947 B1). The following citations refer to WO/0024939. Note that applicant's claim for priority has not been granted as discussed above, and the prior art has been applied based on the instant application filing date (August 6, 2003).

With regard to claim 1, Dong et al. disclose a method of analyzing nucleic acids using the polymerase chain reaction (PCR), comprising:

- a. Providing a double-stranded population of nucleic acids comprising single-stranded overhangs (see page 2, lines 16-20 and Figure 4)
- b. Annealing ligate linkers to said population of nucleic acids whereby at least a subset of nucleic acids from said double-stranded population have linkers bound at both ends (see page 2, lines 16-20 and Figure 4)
- c. Amplifying said subset of nucleic acids by PCR, thereby analyzing said subset of nucleic acids (see page 2, lines 16-25 and Figure 4).

Note that the "adaptor sequences" of Dong et al. are oligonucleotides of 5-60 bases in length and may be ligated to single-stranded overhangs (page 10, lines 3-18). These "adaptor sequences" are therefore a functional equivalent of the instantly claimed "ligate linkers". This disclosure of Dong et al. meets the limitations of the instant claim 1.

With regard to claim 2, Dong et al. disclose the use of the method in analyzing genomic DNA (page 1, lines 25-26), thereby meeting the instant limitation that said population of nucleic acids is a population of genomic DNA fragments.

With regard to claim 3, Dong et al. disclose that said single-stranded overhangs are derived from restriction enzyme digestions (see page 2, lines 16-20 and Figure 4).

With regard to claim 4, Dong et al. disclose that said ligate linkers comprise a common PCR primer binding site (see Example 2, pages 24-25).

With regard to claim 5, Dong et al. disclose that said ligate linkers comprise a different PCR primer binding site for each overhang (see Example 3, pages 25-26).

With regard to claim 6, Dong et al. disclose that said restriction enzyme is selected from the group consisting of a single Type IIs restriction enzyme, a combination of two or more Type IIs enzymes, and a combination of Type IIs restriction enzymes and other types of restriction enzymes. Specifically, Dong et al. disclose the use of a Type IIs restriction enzyme (page 2, lines 23-25).

Conclusion

7. No claims are currently allowable over the prior art.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is (571) 272-8291. The examiner can normally be reached on M-F 7:30-5 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Angela Bertagna *Angela* 12/15/2005
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12/15/05